WHAT IS CLAIMED IS:

1. A method for identifying a polymorphism or combination of polymorphisms associated with an A2M-mediated disease or disorder, comprising testing one or more polymorphisms in an A2M gene individually and/or in combinations for genetic association with an A2M-mediated disease or disorder, wherein the one or more polymorphisms is/are selected from the group consisting of 6i, 12i.1, 12i.2, 12e, 14e, 14i.1, 14i.2, 17i.1, 20e, 20i, 21i, 28i and 30e.

2. A method for identifying a polymorphism or combination of polymorphisms associated with a neurodegenerative disease or disorder, comprising testing one or more polymorphisms in an A2M gene individually and/or in combinations for genetic association with a neurodegenerative disease or disorder, wherein the one or more polymorphisms is/are selected from the group consisting of 6i, 12i.1, 12i.2, 12e, 14e, 14i.1, 14i.2, 17i.1, 20e, 20i, 21i, 28i and 30e.

3. The method of claim 1, wherein the nucleotide at 6i is C or A, the nucleotide at 12i.1 is C or G, the nucleotide at 12i.2 is A or T, the nucleotide at 12e is C or T, the nucleotide at 14e is T or C, the nucleotide at 14i.1 is no insertion or insertion of AAG, the nucleotide at 14i.2 is A or C, the nucleotide at 17i.1 is C or G, the nucleotide at 20e is C or T, the nucleotide at 20i is C or G, the nucleotide at 21i is T or A, the nucleotide at 28i is T or G and the nucleotide at 30e is T or C, or the complementary nucleotide thereof.

4. The method of claim 2, wherein the nucleotide at 6i is C or A, the nucleotide at 12i.1 is C or G, the nucleotide at 12i.2 is A or T, the nucleotide at 12e is C or T, the nucleotide at 14e is T or C, the nucleotide at 14i.1 is no insertion or insertion of AAG, the nucleotide at 14i.2 is A or C, the nucleotide at 17i.1 is C or G, the nucleotide at 20e is C or T, the nucleotide at 20i is C or G, the nucleotide at 21i is T or A, the nucleotide at 28i is T or G and the nucleotide at 30e is T or C, or the complementary nucleotide thereof.

5. The method of claim 2, wherein the disease is Alzheimer's disease.

6. A method of genotyping a cell comprising:

obtaining from an individual a biological sample containing an alpha-2-macroglobulin nucleic acid or portion thereof; and

determining the identity of one or more nucleotides in said alpha-2-macroglobulin nucleic acid or portion thereof wherein said one or more nucleotides are located at a position selected from the group consisting of 6i, 12i.1, 12i.2, 12e, 14e, 14i.1, 14i.2, 17i.1, 20e, 20i, 21i, 28i and 30e.

7. The method of claim 6, wherein said alpha-2-macroglobulin nucleic acid is genomic DNA.

8. The method of claim 6, wherein said alpha-2-macroglobulin nucleic acid is RNA.

9. The method of claim 6, comprising determining the identity of one or more nucleotides at a position selected from the group consisting of 6i, 12e, and 14i.1.

10. The method of claim 9, further comprising determining the identity of one or more nucleotides at a position selected from the group consisting of 18i and 1us.

11. The method of claim 10, comprising determining the identity of one or more nucleotides at each of positions 1us, 6i, 12e, 14i.1 and 18i.

12. The method of claim 6, comprising determining the identity of one or more nucleotides at a position selected from the group consisting of 6i, 12e, 14i.1 and 20e.

13. The method of claim 12, further comprising determining the identity of one or more nucleotides at position 18i.

14. The method of claim 6, comprising determining the identity of one or more nucleotides at a position selected from the group consisting of 6i, 12e, 14i.1 and 21i.

15. The method of claim 14, further comprising determining the identity of one or more nucleotides at a position selected from the group consisting of 18i and 24e.

16. The method of claim 15, comprising determining the identity of one or more nucleotides at each of positions 6i, 12e, 14i.1, 18i and 21i.

17. The method of claim 6, comprising determining the identity of one or more nucleotides at a position selected from the group consisting of 12e, 14i.1 and 21i.

18. The method of claim 17, further comprising determining the identity of one or more nucleotides at a position selected from the group consisting of 18i and 24e.

19. The method of claim 18, comprising determining the identity of one or more nucleotides at each of positions 12e, 14i.1, 18i, 21i and 24e.

20. The method of claim 6, comprising determining the identity of one or more nucleotides at a position selected from the group consisting of 14i.1, 20e and 21i.

21. The method of claim 20, further comprising determining the identity of one or more nucleotides at a position selected from the group consisting of 18i and 24e.

22. The method of claim 6, comprising determining the identity of one or more nucleotides at a position selected from the group consisting of 20e and 21i.

23. The method of claim 22, further comprising determining the identity of one or more nucleotides at a position selected from the group consisting of 18i, 24e and rs1805654.

24. The method of claim 6, comprising determining the identity of one or more nucleotides at a position selected from the group consisting of 14i.1 and 21i.

25. The method of claim 24, further comprising determining the identity of one or more nucleotides at a position selected from the group consisting of 18i, 24e and rs1805654.

26. The method of claim 25, comprising determining the identity of one or more nucleotides at each of positions 14i.1, 18i, 21i, 24e and rs1805654.

27. A method of genotyping a cell comprising:

obtaining from an individual a biological sample containing an alpha-2-macroglobulin polypeptide or portion thereof; and

determining the identity of one or more amino acids in said alpha-2-macroglobulin polypeptide or portion thereof wherein said one or more amino acids are located at a position selected from the group consisting of 14e, 20e and 30e.

28. A method of identifying a subject at risk for Alzheimer's Disease, said method comprising:

obtaining from said subject a biological sample containing an alpha-2-macroglobulin nucleic acid or portion thereof; and

determining the presence or absence of one or more polymorphisms or mutations in said alpha-2-macroglobulin nucleic acid or portion thereof wherein said one or more polymorphisms or mutations occur at a position selected from the group consisting of 6i, 12i.1, 12i.2, 12e, 14e, 14i.1, 14i.2, 17i.1, 20e, 20i, 21i, 28i and 30e.

29. The method of claim 28, wherein said alpha-2-macroglobulin nucleic acid is genomic DNA.

30. The method of claim 28, wherein said alpha-2-macroglobulin nucleic acid is RNA.

31. The method of claim 28, wherein the nucleotide at 6i is C or A, the nucleotide at 12i.1 is C or G, the nucleotide at 12i.2 is A or T, the nucleotide at 12e is C or T, the nucleotide at 14e is T or C, the nucleotide at 14i.1 is no insertion or insertion of AAG, the nucleotide at 14i.2 is A or C, the nucleotide at 17i.1 is C or G, the nucleotide at 20e is C or T, the nucleotide at 20i is C or G, the nucleotide at 21i is T or A, the nucleotide at 28i is T or G and the nucleotide at 30e is T or C, or the complementary nucleotide thereof.

32. The method of claim 28, comprising determining the presence or absence of one or more polymorphisms at a position selected from the group consisting of 6i, 12e, and 14i.1.

33. The method of claim 32, further comprising determining the presence or absence of one or more polymorphisms at a position selected from the group consisting of 18i and 1us.

34. The method of claim 33, comprising determining the presence or absence of one or more polymorphisms at each of positions 1us, 6i, 12e, 14i.1 and 18i.

35. The method of claim 34, wherein the nucleotide at position 1us is G, the nucleotide at position 6i is C, the nucleotide at position 12e is C, the nucleotide at position 14i.1 is insertion of AAG, the nucleotide at position 18i is a pentanucleotide deletion, or the complementary nucleotide thereof.

36. The method of claim 35, wherein the nucleotide at position 1us is G, the nucleotide at position 6i is C, the nucleotide at position 12e is T, the nucleotide at position 14i.1 is insertion of AAG, the nucleotide at position 18i is a pentanucleotide deletion, or the complementary nucleotide thereof.

37. The method of claim 35, wherein the nucleotide at position 1us is T, the nucleotide at position 6i is C, the nucleotide at position 12e is T, the nucleotide at position 14i.1 is insertion of AAG, the nucleotide at position 18i is no deletion, or the complementary nucleotide thereof.

38. The method of claim 28, comprising determining the presence or absence of one or more polymorphisms at a position selected from the group consisting of 6i, 12e, 14i.1 and 20e.

39. The method of claim 38, further comprising determining the presence or absence of one or more polymorphisms at position 18i.

40. The method of claim 28, comprising determining the presence or absence of one or more polymorphisms at a position selected from the group consisting of 6i, 12e, 14i.1 and 21i.

41. The method of claim 40, further comprising determining the presence or absence of one or more polymorphisms at a position selected from the group consisting of 18i and 24e.

42. The method of claim 41, comprising determining the presence or absence of one or more polymorphisms at each of positions 6i, 12e, 14i.1, 18i and 21i.

43. The method of claim 42, wherein the nucleotide at position 6i is C, the nucleotide at position 12e is T, the nucleotide at position 14i.1 is insertion of AAG, the nucleotide at position 18i is no deletion, and the nucleotide at position 21i is A, or the complementary nucleotide thereof.

44. The method of claim 28, comprising determining the presence or absence of one or more polymorphisms at a position selected from the group consisting of 12e, 14i.1 and 21i.

45. The method of claim 44, further comprising determining the presence or absence of one or more polymorphisms at a position selected from the group consisting of 18i and 24e.

46. The method of claim 45, comprising determining the presence or absence of one or more polymorphisms at each of positions 12e, 14i.1, 18i, 21i and 24e.

47. The method of claim 46, wherein the nucleotide at position 12e is T, the nucleotide at position 14i.1 is insertion of AAG, the nucleotide at position 18i is no deletion, the nucleotide at position 21i is A, and the nucleotide at position 24e is A, or the complementary nucleotide thereof.

48. The method of claim 28, comprising determining the presence or absence of one or more polymorphisms at a position selected from the group consisting of 14i.1, 20e and 21i.

49. The method of claim 48, further comprising determining the presence or absence of one or more polymorphisms at a position selected from the group consisting of 18i and 24e.

50. The method of claim 28, comprising determining the presence or absence of one or more polymorphisms at a position selected from the group consisting of 20e and 21i.

51. The method of claim 50, further comprising determining the presence or absence of one or more polymorphisms at a position selected from the group consisting of 18i, 24e and rs1805654.

52. The method of claim 28, comprising determining the presence or absence of one or more polymorphisms at a position selected from the group consisting of 14i.1 and 21i.

53. The method of claim 52, further comprising determining the presence or absence of one or more polymorphisms at a position selected from the group consisting of 18i, 24e and rs1805654.

54. The method of claim 53, comprising determining the identity of one or more nucleotides at each of positions 14i.1, 18i, 21i, 24e and rs1805654.

55. The method of claim 54, wherein the nucleotide at position 14i.1 is insertion of AAG, the nucleotide at position 18i is a pentanucleotide deletion, the nucleotide at position 21i is T, the nucleotide at position 24e is A, and the nucleotide at position rs1805654 is G, or the complementary nucleotide thereof.

56. The method of claim 28, comprising determining the presence or absence of one or more polymorphisms at a position selected from the group consisting of 12e, 14i.1, and 21i.

57. The method of claim 56, wherein the nucleotide at position 12e is T, or the complement thereof, the nucleotide at position 14i.1 is AAG insertion, or the complement thereof, and the nucleotide at position 21i is T.

58. A method of identifying a subject at risk for Alzheimer's Disease, said method comprising:

obtaining from said subject a biological sample containing an alpha-2-macroglobulin polypeptide or portion thereof; and

determining the presence or absence of one or more polymorphisms or mutations in said alpha-2-macroglobulin polypeptide or portion thereof wherein said one or more polymorphisms or mutations occur at a position selected from the group consisting of 14e, 20e and 30e.

59. A method of identifying a compound that modulates an alpha-2-macroglobulin activity comprising:

providing a plurality of cells that express the LRP receptor;

contacting said cells with a candidate compound;

contacting said cells with an alpha-2-macroglobulin polypeptide comprising at least one polymorphism or mutation having a position selected from the group consisting of 14e, 20e, and 30e; and

identifying a compound that modulates an alpha-2-macroglobulin activity.

60. The method of claim 59, wherein said alpha-2-macroglobulin activity is an interaction of said alpha-2-macroglobulin polypeptide with the LRP receptor.

61. The method of claim 59, wherein said alpha-2-macroglobulin activity is the degradation of said alpha-2-macroglobulin polypeptide.

62. The method of claim 59, wherein said alpha-2-macroglobulin activity is a protease inhibitor activity.

63. The method of claim 59, wherein said alpha-2-macroglobulin activity is the clearance of said alpha-2-macroglobulin polypeptide.

64. The method of claim 59, wherein said cells are contacted with an alpha-2-macroglobulin polypeptide in the presence of amyloid β.

65. The method of claim 64, wherein said alpha-2-macroglobulin activity is an interaction of amyloid b or said alpha-2-macroglobulin polypeptide with the LRP receptor.

66. The method of claim 65, wherein said alpha-2-macroglobulin mediates clearance of amyloid β.

67. A method of identifying a compound that modulates an alpha-2-macroglobulin activity comprising:

providing an alpha-2-macroglobulin polypeptide comprising at least one of the polymorphisms or mutations having a position selected from the group consisting of 14e, 20e, and 30e;

contacting said alpha-2-macroglobulin polypeptide with said compound;

contacting said alpha-2-macroglobulin polypeptide with methylamine; and

identifying a compound that modulates an alpha-2-macroglobulin activity by detecting a modulation in the activation of said alpha-2-macroglobulin polypeptide.

68. A method of identifying a compound that modulates an alpha-2-macroglobulin activity comprising:

providing an alpha-2-macroglobulin polypeptide comprising at least one of the polymorphisms or mutations having a position selected from the group consisting of 14e, 20e, and 30e;

contacting said alpha-2-macroglobulin polypeptide with said compound;

contacting said alpha-2-macroglobulin polypeptide with amyloid b; and

identifying a compound that modulates an alpha-2-macroglobulin activity by detecting a modulation in the formation of a complex of amyloid β and said alpha-2-macroglobulin polypeptide.

69. A method of making a pharmaceutical comprising:

identifying a compound by the method of claim 59 incorporating said compound into a pharmaceutical.

70. A purified or isolated nucleic acid comprising an alpha-2-macroglobulin sequence having a polymorphism or mutation at a position selected from the group consisting of 6i, 12i.1, 12i.2, 12e, 14e, 14i.1, 14i.2, 17i.1, 20e, 20i, 21i, 28i and 30e, wherein the nucleotide or nucleotide sequence at said position is other than an *A2M-1*.

71. The purified or isolated nucleic acid of claim 70, wherein said alpha-2-macroglobulin sequence is SEQ ID NO: 1 or a sequence complementary thereto.

72. The purified or isolated nucleic acid of claim 71, wherein the nucleotide or nucleotide sequence at said position is *A2M-2*.

73. The purified or isolated nucleic acid of claim 70, wherein said alpha-2-macroglobulin sequence is selected from the group consisting of SEQ ID NOs: 2-8 and

said polymorphism or mutation is at a position selected from the group consisting of 14e, 20e and 30e.

74. The purified or isolated nucleic acid of claim 73, wherein the nucleotide or nucleotide sequence at said position is *A2M-2*.

75. The purified or isolated nucleic acid comprising a fragment of at least 16 consecutive nucleotides of SEQ ID NO: 1 having a polymorphism or mutation at a position selected from the group consisting of 6i, 12i.1, 12i.2, 12e, 14e, 14i.1, 14i.2, 17i.1, 20e, 20i, 21i, 28i and 30e, wherein the nucleotide or nucleotide at said position is other than an *A2M-1* or a sequence complementary thereto.

76. The purified or isolated nucleic acid of claim 75, wherein the nucleotide or nucleotide sequence at said position is *A2M-2*.

77. A purified or isolated polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 9-15 having a polymorphism or mutation at a position selected from the group consisting of 14e, 20e and 30e, wherein the amino acid at said position is other than A2M-1.

78. The purified or isolated polypeptide of claim 77, wherein the amino acid at said position is A2M-2.

79. A purified or isolated polypeptide comprising a fragment of an amino acid sequence selected from the group consisting of SEQ ID NOs: 9-15 having a polymorphism or mutation at a position selected from the group consisting of 14e, 20e and 30e, wherein the amino acid mutation at said position is other than A2M-1.

80. The purified or isolated polypeptide of claim 79, wherein the amino acid at said position is A2M-2.

81. A recombinant vector comprising the nucleic acid of claim 75.

82. A cultured cell comprising the nucleic acid of claim 75.

83. A cultured cell comprising the polypeptide of claim 79.

84. A cultured cell comprising the recombinant vector of claim 81.

85. An isolated or purified antibody that specifically binds to the polypeptide of any one of claim 79.

86. The antibody of claim 85, wherein said antibody is monoclonal.

87. A method of expressing an alpha-2-macroglobulin polypeptide comprising:

providing a construct comprising a promoter operably linked to an alpha-2-macroglobulin nucleic acid having a polymorphism or mutation at a position selected from the group consisting of 14e, 20e and 30e, wherein the nucleotide at said position is other than an *A2M-1*; and

expressing said alpha-2-macroglobulin from said construct.

88. The method of claim 87, wherein said nucleotide at said position is *A2M-2*.